DEPARTMENT OF HEALTH AND HUMAN SERVICE

937984

Food and Drug Administration
New Orleans District
Southeast Region
6600 Plaza Drive, Suite 400
New Orleans, Louisiana 70127

Telephone: 504-253-4519
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November 5, 2002

WARNING LETTER NO. 2003-NOL-03

FEDERAL EXPRESS
OVERNIGHT DELIVERY

Alberto Martinez, Jr., M.D.
Senior Vice President and General Manager
Aventis Bio-Services, Inc.
1020 1st Avenue
King of Prussia, Pennsylvania 19406

Dear Dr. Martinez:

During an inspection of your plasmapheresis center, located at 3511 A Desiard Street, Monroe, Louisiana on July 15 - 19, 23 - 27 & August 9, 2002, our investigator documented deviations from Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act) and the Current Good Manufacturing Practice (CGMP) regulations for blood and blood components and finished pharmaceuticals under Title 21, *Code of Federal Regulations* (CFR), Parts 210-211 and 600-680. You can find the Act and the other regulations through links in FDA's home page at http://www.fda.gov.

Our investigator documented deficiencies in your firm's training program, including associated employee training records [21 CFR 606.20(b) and 21 CFR 211.25(a)]:

- Your plasma processing employees were observed performing plasma collection duties, such as disconnecting phlebotomies, for which they are not trained or prior to completing their training; and,

- You did not retain employee competency test documentation as required by your standard operating procedures (SOPs).

Numerous deficiencies were documented relating to your firm's failure to follow written SOPs [21 CFR 211.100 and 606.100].

1. Your firm's employees did not document each significant step during the disposal of unsuitable units in accordance with your written procedures:

- Your employees did not document the disposal of unit 005061, collected from an HIV positive donor, on the "Unacceptable Plasma Record" which documents: the reason for disposal, who removed the unit from the freezer, who placed the unit in the medical waste container, who verified the disposal, and the collection of the unit by the medical waste service; and,

- Your employees did not document the disposal of unit 076162, collected from an indeterminate HIV positive donor, on the "Unacceptable Plasma Record."

2. Your firm failed to act on post donation information reports on an expedited basis and conduct a recall of units as required by your SOPs:

   - Donor [redacted] was deemed to be at risk for hepatitis and HIV infection because the donor provided unreliable medical history regarding their pierced ears on May 2, 2002, and your firm did not initiate a recall of distributed products until July 29, 2002;

   - Donor [redacted] tested positive for drugs on June 10, 2002, and your firm did not initiate a recall of distributed products until August 7, 2002; and,

   - Donor [redacted] was deemed to be at risk for hepatitis and HIV infection because the donor provided unreliable medical history regarding their pierced ears on May 2, 2002, and your firm did not initiate a recall of distributed products until July 23, 2002.

3. Your firm did not list temporarily deferred donors (03737 and 08116) in your Deferred Donor Record file in accordance with your written procedures.

4. Your employees did not follow your SOP's pertaining to review of records:

   - A second employee did not verify the Donor Sample/Plasma Packing Lists on June 5 and 6, 2002;

   - Numerous Donor Sample/Plasma Packing lists were verified by employees other than the Center Manager or Quality Assurance Specialist (QAS)/designee as required by your SOP;

   - Employees other than the QAS verified that unacceptable units were removed from the freezer, as required by your SOP; and,

   - Records documenting the manufacture of plasma were not reviewed by a second knowledgeable employee. For example, the same person performed the task of disposing unacceptable units and also performed the QAS review of the records documenting those actions.

5. Your firm did not record post donation information on the Post Donor Information (PDI) Sequential Number log for donors [redacted] and [redacted] in accordance with your written procedures.

Your firm reported 11 Biological Product Deviation reports to the U.S. Food and Drug Administration, between April 30 and June 17, 2002, in excess of 45 days of discovering the event [21 CFR 600.14(c)].

The above deviations are not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure that all source plasma produced and issued by your plasmapheresis center is in compliance with the Act and with the CGMP regulations. You should take prompt action to correct these deviations. Your failure to correct these deviations may result in regulatory action being taken by FDA without further notice. Possible actions include license suspension and/or revocation, seizure, and/or injunction.

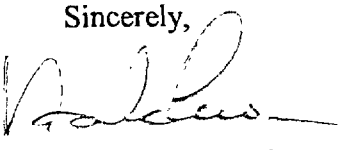
We are in receipt of your written response, dated September 17, 2002, to the inspectional observations discussed with your employees. We have reviewed your response, and note you have committed to a number of corrective actions to address the observations, including revisions to procedures, hiring of additional staff, and re-training of current staff. However, your response provided no documentation to demonstrate that SOPs have been appropriately revised to reflect the new procedures and employees have been trained on the revised procedures. In your response to this letter, we request that you provide complete documentation to demonstrate the promised corrective actions have been appropriately implemented. In addition, we have the following specific comment on your response:

1. Observation #15 concerned the lack of documentation of employee competency tests, as it was your firm's practice to discard the test after grading. In your response, you state that a new SOP has been developed that requires all tests to be retained in the personnel training files. Your response does not address whether current employees will be re-tested in order to complete their documentation of training in accordance with the new SOP.

We request that you notify this office in writing, within fifteen (15) working days of receipt of this letter, of specific steps you have taken to correct these deviations, including examples of any documentation such as employee training records, written standard operating procedures or other records demonstrating corrective action. If you cannot complete corrections within 15 working days, state the reason for the delay and the time period within which corrections will be completed.

Your reply should be directed to Mark W. Rivero, Compliance Officer, at the above address.

Sincerely,



Howard E. Lewis
Acting District Director
New Orleans District

Enclosure: Form FDA 483